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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,574	05/31/2007	Stig Bengmark	05822.0340USWO	8316

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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
12/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,574	BENGMARK, STIG	
	Examiner	Art Unit	
	Kade Ariani	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 12-26 are pending in this application and were examined on their merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-16, and 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaur et al. (European Journal of Pharmaceutical Sciences, 2002, Vol. 15, p.1-9) in view of Kruszewskya et al. (in IDS, Microecology and Therapy, 2002, Vol. 29, p.37-49) and further in view of Naito et al. (Free Radical Biology & Medicine, 2002, Vol. 33, No. 3, p.323-336).

Claims 12-16, and 20-26 are drawn to a method for treating a stress-induced inflammatory disorder in a mammal, comprising administering to a mammal in need of treatment an effective amount of a formulation comprising at least 10^6 CFU/ml of each of *Pediococcus pentoseceus 16:1(LMG P-20608), Leuconostoc mesenteriodes 23-77:1 (LMG P-20607), lactobacillus paracasei subsp paracasei F-19 (LMG P-17086), and Lactobacillus plantarum 2362 (LMG P-20606),* and at least one fiber, the mammal is a human, wherein the stress-induced disorder is determined as an increase in

neutrophils, cytokines, myeloperoxidases, the stress induced disorder is stomach inflammation, bowel inflammation, the fiber is inulin, the formulation further comprises at least one antioxidant, vitamin, amino acid, peptide, glutamine, the formulation further comprises a therapeutic agent, the formulation is solid or liquid, the formulation is in the form of a tablet, the formulation comprises at least 10^{10} CFU of each bacteria, and at least 10^{11} CFU/ml of each bacteria.

Kaur et al. teach a method for treating a stress induced inflammatory disorder, treating ulcers related to *H. pylori* (it must be noted that *H. pylori* induce gastric inflammation, a stress-induced inflammation, see Naito et al. Abstract) and colitis (p.1 Introduction 1st column lines 9 and 15-16). Kaur et al. also teach probiotic formulation comprising a combination of probiotic strains for treating ulcerative colitis (a stress-induced inflammation and bowel inflammation) in a mammal in need, at least 10^{11} cells/g of strains ($5X10^{11}$ cells of strains), in the form of tablets and capsules (p.4 Table 1. VSL# 3, and p.5 Table 1. Continued 1st column Primal Defense capsules). Kaur et al. further teach synbiotics (a mixture of probiotics and prebiotics, non-digestible food ingredients) overcome the limitations of probiotics and improve the survival and implantation of live microbial dietary supplement (p.7 2nd column 2nd paragraph). Kaur et al. teach combined administration of inulin with a probiotic (p. 6 7 2nd column 3rd paragraph). Kaur et al. teach including vitamins, antioxidants, minerals, plants (wheat, barley, soybean), and formulation comprises wheat and barley, and therapeutic agents (e.g. amoxycillin), in the formulation (p.5 Table 1. continued, 2nd column 3rd paragraph line 17, 3rd column 3rd paragraph lines 10-11, and 3rd column 1st paragraph). Kaur et al.

further teach a well-established fact is that by probiotic therapy resistant to pathogen and immune stimulation (non-specific immune response) can be achieved (p.7 1st column last paragraph, and p.5 2nd column 2nd paragraph).

Kaur et al. do not teach wherein the stress-induced disorder is determined as an increase in neutrophils, cytokines, myeloperoxidases, a formulation comprising an effective amount of *Pediococcus pentosaceus 16:1(LMG P-20608), Leuconostoc mesenteriodes 23-77:1 (LMG P-20607), lactobacillus paracasei subsp paracasei F-19 (LMG P-17086), and Lactobacillus plantarum 2362 (LMG P-20606)*, and glutamine. However, Naito et al. teach *H. pylori* induce gastric inflammation, is a stress-induced inflammation, the bacteria or their products trigger inflammatory process via cytokines (Abstract). Naito et al. teach activation of neutrophils and myeloperoxidase (p.325 1st column 2nd paragraph). Naito et al. further teach accumulation of lipid peroxidation products in *H. pylori*-infected gastric mucosa provides evidence of increased oxidative stress (p.326 1st column 1st paragraph lines 8-12).

Moreover, Kruszewskya et al. teach *Pediococcus pentosaceus 16:1, Leuconostoc mesenteriodes 77:1, lactobacillus paracasei subsp paracasei F-19, and Lactobacillus plantarum 2592* have shown properties which makes them attractive candidates for use as probiotics (Abstract, page 41 Table 2.). Kruszewskya et al. teach the strains produce bacteriocins with bactericidal effect against bacterial species like *H. pylori* (p.44 1st column 3rd paragraph lines 1-4). Kruszewskya et al. teach the strains grown/cultured in a nutrient medium with 0.5% w/v inulin, amylopectin, beta-glucan, and with L-glutamine (p.40, 2nd column 2nd paragraph line 8). Kruszewskya et al. also teach

the strains are isolated from cultured rye (Abstract line 3). Kruszewskya et al. teach the production of antimicrobial substances (with activity against other bacteria) by these strains, induction of anti-inflammatory cytokines (IL-10) by *L. paracasei subsp paracasei F-19*, *Lactobacillus plantarum 2592*, *Pediococcus pentosaceus 16:1* produced antioxidants which provide beneficial effects in scavenging free radicals (Abstract and p.45 1st and 2nd columns). Kruszewskya et al. teach the strains ferment fibers and exert beneficial effect of the colonic flora and bowel function (p.44 2nd column 2nd paragraph).The LAB strains taught by Kruszewskya et al. are the same or in case of *Lactobacillus plantarum 2592*, an obvious variant of the claimed bacterial strains. Kruszewskya et al. teach the induction of IL-8 (pro-inflammatory) and IL-10 (antiinflammatory) cytokines, and a mild immunostimulatory effect by *lactobacillus paracasei subsp paracasei F-19* (p.45 1st column 2nd paragraph lines 1-4). It must be noted that IL-8 is a mediator of the immune reaction in the innate immune system response which provide immediate defense against infection and is not long lasting. Kruszewskya et al. also teach the tetsted strains ferment fibers, they should exert a benebeficial effect on the colonic flora, and possibly act as a prebiotic since they fermnet inulin, which has been shown to stimulate the growth of Bifidobacteria (p.44 2nd column 2nd paragraph). Kruszewskya et al. also teach the selected LAB strains have shown to survive and multiply during the acid and bile stress conditions of human stomach and upper intestine and they have a prominent ability to colonise the human large intestine (p.43 2nd column last paragraph and p.44 1st column 1st paragraph). It

must be noted that a probiotic must be capbale of colonizing the intestinal tract to influence human health.

Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to provide a formulation by combining the probiotic strains, *Pediococcus pentosaceus 16:1, Leuconostoc mesenteriodes 77:1, lactobacillus paracasei subsp paracasei F-19, and Lactobacillus plantarum 2592* as taught by Kruszewskya et al. in an effective amount and at least one fiber according to the teachings of Kaur et al., because Kaur et al. teach combination of probiotic strains in an effective amount with fiber for treating a stress-induced inflammation. A person of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in administering a formulation of the combination of probiotic strains in effective amount with fiber for treating stress-induced disorder/*H. pylori* induced gastric inflammation as taught by Kaur et al. and Naito et al. in order to provide a method of treating a stress-induced inflammatory disorder because Kruszewskya et al. teach the probiotic strains, *Pediococcus pentosaceus 16:1, Leuconostoc mesenteriodes 77:1, lactobacillus paracasei subsp paracasei F-19, and Lactobacillus plantarum 2592*, produce bacteriocins with bactericidal effect against bacterial species like *H. pylori*. As indicated in MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations

omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious).

Claims 12 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaur et al. (European Journal of Pharmaceutical Sciences, 2002, Vol. 15, p.1-9) in view of Kruszewskya et al. (in IDS, Microecology and Therapy, 2002, Vol. 29, p.37-49) and further in view of Gibson et al. (J Nutr., 1999, Vol. 129, p.1438S-1441S) and Charalampopoulos et al. (International Journal of Food Microbiology, 2002, Vol. 79, p.131-141).

Claims 12, and 17-19 are drawn to a method for treating a stress-induced inflammatory disorder in a mammal, comprising administering to a mammal in need of treatment an effective amount of a formulation comprising at least 10^6 CFU/ml of each of *Pediococcus pentoseceus 16:1(LMG P-20608), Leuconostoc mesenteriodes 23-77:1 (LMG P-20607), lactobacillus paracasei subsp paracasei F-19 (LMG P-17086), and Lactobacillus plantarum 2362 (LMG P-20606),* and at least one fiber, wherein the fibers

are inulin, beta-glucan, pectin, and resistant starch, the fibers in the formulation in an amount of 2.5 g, and the fiber is lignin substances from a plant.

Kaur et al. teach a method for treating a stress induced inflammatory disorder, treating ulcers related to *H. pylori* (it must be noted that *H. pylori* induce gastric inflammation, a stress-induced inflammation, see Naito et al. Abstract) and colitis (p.1 Introduction 1st column lines 9 and 15-16). Kaur et al. teach probiotic formulation comprising a combination of probiotic strains for treating ulcerative colitis (a stress-induced inflammation/bowel inflammation) in a mammal, at least 10^{11} cells/g of strains ($5X10^{11}$ cells of strains), in the form of tablets and capsules (p.4 Table 1. VSL # 3 and p.5 Table 1. Continued 1st column Primal Defense capsules). Kaur et al. further teach synbiotics (a mixture of probiotics and prebiotics, non-digestible food ingredients) overcome the limitations of probiotics and improve the survival and implantation of live microbial dietary supplement (p.7 2nd column 2nd paragraph). Kaur et al. teach combined administration of inulin with a probiotic (p. 6 7 2nd column 3rd paragraph).

Kaur et al. do not teach *Pediococcus pentosaceus 16:1(LMG P-20608), Leuconostoc mesenteriodes 23-77:1 (LMG P-20607), lactobacillus paracasei subsp paracasei F-19 (LMG P-17086), and Lactobacillus plantarum 2362 (LMG P-20606),* 2.5 gram of each fiber, fibers comprises glucan, pectin, resistant starch, and the fiber is selected from lignin substances from a plant. However, Kruszewskya et al. teach *Pediococcus pentosaceus 16:1, Leuconostoc mesenteriodes 77:1, lactobacillus paracasei subsp paracasei F-19, and Lactobacillus plantarum 2592* have shown properties which makes them attractive candidates for use as probiotics (Abstract, page

41 Table 2.). Kruszewskya et al. teach the strains produce bacteriocins with bactericidal effect against bacterial species like *H. pylori* (p.44 1st column 3rd paragraph lines 1-4) (It must be noted that *H. pylori* induced infection is a stress-induced disorder). Kruszewskya et al. teach the strains grown/cultured in a nutrient medium with 0.5% w/v inulin, amylopectin, beta-glucan (p.40, 2nd column 2nd paragraph line 8). Kruszewskya et al. also teach the strains are isolated from colonic mucosa of healthy individuals and from cultured rye (Abstract line 1-3).

Gibson et al. teach a marked increase in bifidobacteria by adding15g/d inulin in the diet of human volunteers (p.1440S 1st column Table 2. legend, and 1st column 2nd paragraph lines 15-24).

Charalampopoulos et al. teach encapsulation of probiotic strains using cereal fractions to improve the viability of the probiotic strains (p.138 2nd column 1st paragraph lines 1-4). Charalampopoulos et al. teach cereals are generally suitable substrates for the growth-of human derived probiotic strains (p. 138 1st column end paragraph). Charalampopoulos et al. also teach the prebiotic effect of cereals due to the presence of dietary fibers, and teach cereals also contain phytic acid (phytate) and tannins (p.136 2nd column 2nd paragraph line1, and 1st column 2nd paragraph lines 2-8). Charalampopoulos et al. teach water soluble fiber and water-insolube fiber contains lignin, cellulose and hemicellulose (p.136 2nd column 1st paragraph lines 2-3). Charalampopoulos et al. teach the most important dietary fiber is beta-glucan which has positive therapeutic effects, and support the growth of lactobacilli and bifidobacteria (p.137 1st column 1st paragraph lines 4-6). Charalampopoulos et al. further teach the

fiber resistant starch (found in cereal grains) is a prebiotic; it provides fermentable carbohydrates for colonic bacteria, and decreases the risk of bowel diseases (p.138 1st column 3rd paragraph lines 1-, and 12-14).

Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to provide a formulation by combining the probiotic strains, *Pediococcus pentosaceus 16:1, Leuconostoc mesenteriodes 77:1, lactobacillus paracasei subsp paracasei F-19, and Lactobacillus plantarum 2592* as taught by Kruszewskya et al. in an effective amount and at least one fiber according to the teachings of Kaur et al., because Kaur et al. teach combination of probiotic strains in an effective amount with fiber for treating a stress-induced inflammation. Moreover, a person of ordinary skill in the art at the time the invention was made would have been motivated to include fibers amylopectin and beta-glucan to the combination of probiotic strains of Kruszewskya et al. to provide a formulation, because Kruszewskya et al. teach strains grow on amylopectin and beta-glucan. Accordingly, a person of ordinary skill in the art at the time the invention was made would have been motivated to add fiber resistant starch and a fiber from a plant according to the teachings of Charalampopoulos et al. to the combination of probiotic strains of Kruszewskya et al. to provide a formulation, because Charalampopoulos et al. teach cereal grains and resistant starch as prebiotics. Moreover, a person of ordinary skill in the art at the time the invention was made would have been capable of optimizing the amount (grams) of fibers to be added to the probiotic strains as taught by Kruszewskya et al., according to the teachings of Kruszewskya et al. and Gibson et al., because Kruszewskya et al.

teach adding 0.5% w/v inulin, amylopectin, beta-glucan to the growth medium of the probiotic strains, and Gibson et al. teach adding15g/d inulin in the diet of human volunteers.

Applicant may submit evidence or arguments that:

A) one of ordinary skill in the art could not have combined the claimed elements by known methods (e.g. due to technological difficulties);

B) the elements in combination do not merely perform the function that each element performs separately; or

C) the results of the claimed combination were unexpected.

Answer to Arguments

Applicant's arguments filed on 08/21/2009 have been fully considered but they are not persuasive.

Applicant argues that Kruszewskya et al. disclose the strains produce bacteriocins with bactericidal effect against *H. pylori* and the only conclusion that may possibly b drawn from this teaching is that an H. pylori infection may be treated by the use of strains taught by Kruszewskya et al. This argument is not found persuasive, because as mentioned immediately above, *H. pylori* induced ulcer is a stress-induced inflammatory disorder, and since Kruszewskya et al. disclose the strains produce bacteriocins with bactericidal effect against *H. pylori*, therefore a person of ordinary skill in the art, recognizing the ability of the strains to produce bacteriocins with bactericidal

effect against *H. pylori*, would have been motivated to use these strains to treat ulcer related to *H. pylori* (a stress-induced disorder).

Applicant argues that a person of ordinary skill in the art would not have been motivated to use *L. paracasei* F19 because of its mild immunostimulatory effect, this argument is not found persuasive because Kruszewskya et al. teach *L. paracasei* F19 produce bacteriocins with bactericidal effect against *H. pylori* and *L. paracasei* F19 exert a mild immunostimulatory effect, but also produce IL-10 which has anti-stimulatory effect and further teach *L. paracasei* F19 produce antioxidants, it must be noted that antioxidant are free radical scavengers which are produced as a result of IL-8 production. Therefore, a person of ordinary skill in the art at the time the invention was made, would have known that *L. paracasei* F19 exert an immunomodulatory role due to the production of both pro-and anti-inflammatory cytokines (see page 6, 1st column 3rd paragraph of Ljungh et al.) and also the antioxidant production by *L. paracasei* F19 was useful against oxidative stress-induced inflammation.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on IFP.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651